REMARKS

I. Status Summary

Claims 1-4, 7-10, and 58-68 are pending in the subject U.S. patent application and have been examined by the United States Patent and Trademark Office (hereinafter "the Patent Office") in a Final Official Action dated January 22, 2009 (hereinafter the "Official Action"). Claims 61-68 have been withdrawn as being directed to non-elected subject matter. Claims 1-4, 7-10, and 58-60 presently stand rejected.

Claims 1, 7, and 58-61 have been amended. New claims 69 -71 have been added. Support for the amendments and new claims can be found in the instant application as originally filed. No new matter has been added.

II. Claim Amendments

Claims 1, 7, and 58 have been amended herein.

More particularly, claims 1 and 7 have been amended to spell out the term "primordial germ cell." Support for the amendment can be found in the instant specification at page 48, line 2.

Claims 1 and 7 have been amended to recite "antigen associated with primordial germ cells development." Support for these amendments can be found throughout the instant specification, for example at page 12, line 1; page 13, lines 11 and 26-28; page 25, lines 8-11; and page 35, lines 21-23.

Claims 1, 7, and 58 have also been amended to more clearly describe the presently claimed subject matter. The preambles of the claims have been amended to replace the word "modulating" with "decreasing" or "inhibiting." The last clause in each claim has been rewritten to more clearly describe the subject matter. Support for these amendments can be found throughout the instant specification, including at least in claims 1 and 7 as originally filed. See also page 33, lines 20-27, of the instant specification.

As such, no new matter has been added by the amendments to the claims.

Reconsideration of the application as amended and in view of the remarks presented hereinbelow is respectfully requested.

III. Objections to the Claims

Claims 1 and 7 have been objected to for reciting the abbreviation "PGC". As stated above, claims 1 and 7 have been amended to spell out the phrase "primordial germ cell." Applicants believe the amendment obviates this rejection. Accordingly, it is respectfully submitted that the objection should now be withdrawn.

IV. Response to the Enablement Rejection

Claims 1-4, 7-10, and 58-60 have been rejected under 35 U.S.C. § 112, first paragraph, upon the contention that the specification does not enable the full scope of the claims. After careful consideration of the rejection and the Patent Office's basis therefor, applicants respectfully traverse the rejection and submit the following remarks.

In support of the instant rejection, the Patent Office presents three general assertions that it alleges support the instant rejection. These three general assertions can be summarized as follows:

(A) the specification fails to provide an enabled use for decreasing PGCs without producing a chimeric avian;

(B) the specification fails to teach how to determine whether amounts of antigens or antibodies that decrease endogenous PGCs had been injected or obtained without sacrificing the embryo;

(C) the specification does not enable using any antigen "associated with" PGCs as broadly claimed.

Turning first to Assertion (A), the Patent Office asserts that the sole disclosed use for decreasing PGCs in an avian embryo is to repopulate the embryo with donor PGCs to make a chimeric avian, and thus chimera formation is an essential step in the method.

Applicants respectfully disagree. The methods of claims 1, 7, and 58 can be used to generate PGC-depleted embryos that can be employed as a starting point for creating different types of chimeric avians. As is explained in Example 3, page 57, line 12, of the instant Specification, the eggs containing PGC-depleted embryos (produced by the methods of claims 1, 7, and 58) can be repopulated with donor PGCs at

developmental stage 14-17 of the Hamburger & Hamilton staging system. One having skill in the art knows that this time frame corresponds to about 50-64 hours after the egg was laid. Such PGC-depleted embryos can be sold and shipped during this at least four day period to a user who can use the product of the methods as he/she sees fit including to repopulate the embryo with proprietary transgenic PGCs (Specification, page 37, lines 20-22) or with PGCs from any number of different endangered species (Specification, page 14, lines 7-9).

Applicants respectfully submit that the claimed methods clearly do have an enabled use (*i.e.*, the production of a PGC-depleted avian embryo) and that the products of the methods are useful in and of themselves.

Furthermore, applicants respectfully submit that "if any use is enabled when multiple uses are disclosed, the application is enabling for the claimed invention." M.P.E.P. § 2164.01(c); *see also* Ex Parte Usman, 2002 WL 33948431, at 6 (Bd.Pat.App. & Interf. 2002) (unpublished).

Still further, on page 7, lines 5-7, of the Official Action, the Patent Office contends that the "method under consideration" (presumably the methods of claims 1, 7, and 58 generally drawn to a method of decreasing the number of or inhibiting PGCs in an embryo) is a subcombination in a combination/subcombination relationship with the inventions of groups III and IV (methods of producing a chimeric avian). The Patent Office also contends that "[A]pplicants' arguments regarding [the utility of] using the methods to make chimeric chickens cannot be considered because such methods relate to a patentably distinct method which applicants elected without traverse." *See* Official Action, sentence bridging page 6-7.

Applicants respectfully disagree and submit that the Patent Office's contention that electing without traverse is an admission of distinct utility among restriction groups has not been supported in any authority. Furthermore, according to MPEP 806.05(c)(B), a combination and subcombination are distinct if the subcombination can be shown to have utility either by itself or in another materially different combination. Otherwise the inventions are not distinct. Therefore, if the Patent Office maintains the restriction between combination and subcombination, the Patent Office must find that the subcombination has utility. Applicants maintain that it is useful to create a PGC-

depleted embryo, whether it is used as a commodity at that stage, used to produce a chimeric avian, or both.

In the Official Action, page 5, lines 16-18, the Patent Office maintains that "repopulating the embryo with donor PGCs and obtaining a chimeric avian are essential steps to the method claimed." In response to applicants remarks to this assertion, submitted with Amendment C filed October 29, 2009, the Patent Office states, "Applicants' arguments regarding intermediate/final products fail to apply to the methods claimed; products do not correlate to methods." (Official Action, page 7, lines 3-4).

Applicants disagree and respectfully submit that the Patent Office has misread applicants' response accompanying Amendment C. Therein, applicants provided examples of recently issued patents, U.S. Patent Nos. 6,951,955 and 7,078,572 which claim methods for the synthesis of intermediates (aldehydes). Applicants' point was that under current U.S. law, methods for producing intermediates are clearly patentable subject matter. Applicants also cited *Eastman Chemical Co., v. BASF Aktiengesellschaft* 2000 WL 1897258 (E.D.Tenn.), *aff'd.* 47 Fed. Appx. 566 (Fed. Cir. 2002), regarding U.S. Patent No. 5,118,856 with claims to methods for preparing intermediates (cyclohexanedione derivatives). Therein, the District Court found no known use for the cyclohexanedione derivatives other than as chemical intermediates (*see* FN1 of *Eastman Chemical Co.*). Applicants respectfully maintain that this case clearly demonstrates the fact that, even though the cyclohexanedione derivatives can only be used for producing herbicides, the further step of synthesizing a herbicide was not an essential step that needed to be recited in the claimed method.

Therefore, applicants respectfully submit that it is clear under U.S. patent law that claims to methods for producing an intermediate can be patentable subject matter when the intermediate can be used for producing a downstream composition with known utility. In the instant context, the intermediate can be a PGC-depleted avian embryo, which can then be used to produce a chimeric avian. As with the '955, '572, and '856 Patents, the steps that can be used for producing the downstream composition (*e.g.*, the chimeric avian), are not properly considered essential steps in the method for producing the intermediate (*e.g.*, the PGC-depleted avian embryo), and thus need not be recited in the claimed methods.

As a result, applicants respectfully submit that the Patent Office's apparent contention, that using the intermediate (*i.e.*, the PGC-depleted embryo) for producing the end product (for example, a chimeric avian) would be an essential step under enablement analysis, has not been supported in any authority, and thus is believed to be improper.

The Patent Office also contends that the "PGC numbers can increase or increase." (Official Action, page 7, line 13). Applicants respectively submit that with a full reading of the methods currently under examination (claims 1, 7, and 58), one will see that the amended claims recite that the PGC numbers decrease ("wherein endogenous Primordial Germ Cell numbers in the avian embryo are decreased," "wherein development of Primordial Germ Cells in the avian embryo is inhibited," or "wherein primordial germ cell development is inhibited"). To further clarify this issue, and as discussed in the amendments to the claims above, these claims have been amended to replace the word "modulating" with "decreasing" or "inhibiting," as is also recited in the last clause of each claim.

Accordingly, for the reasons stated above, applicants respectfully submit that Assertion (A) fails to support the instant rejection under 35 U.S.C. § 112, first paragraph.

Turning now to Assertion (B), the Patent Office asserts that the specification fails to teach how to determine whether amounts of antigens or antibodies that decrease endogenous PGCs had been injected or obtained without sacrificing the embryo. The Patent Office also asserts that the specification does not teach how to use breeding techniques to assay PGC numbers (Official Action, page 8, lines 11-12). Applicants respectfully disagree and submit that this assertion also fails to support the instant rejection for at least the following reasons.

First, the experiments that are explicitly disclosed in the specification indicate that immunizing female avians with antigens associated with PGCs resulted in at least a 35% reduction in PGC numbers in the embryos. This was indeed determined by sacrificing the embryos, but applicants respectfully submit that once it is shown that immunizing the female avians predictably resulted in decreased PGC numbers, one having skill in the art would have no need to test each and every embryo for a similar

result. The Patent Office has identified no reasonable scientific basis for its assertion that the decrease in PCG numbers observed in the embryos disclosed in Example 2 of the instant specification would not also occur in other embryos that experienced the same treatment, such as those used in Example 3 (Specification, page 57, lines 8-9) to repopulate the PGC-depleted embryos with donor cells, or in Examples 4 (*Id.*, page 59, lines 5-6), and 5 (*Id.*, page 60, line 10) to produce avian chimeras.

Example 5 describes that embryos are treated to deplete PGCs, using the protocols described in the earlier examples. These same embryos then receive donor PGC's, are allowed to hatch and are used in breeding. Pigment markers observed in the offspring of the treated (PGC-depleted) birds but not observed in the offspring of the untreated (control) birds indicate transmission of gametes derived from the donor PGC's. One of ordinary skill in the art understands that obtaining more pigmented chicks in the offspring population demonstrates that sufficient antigen was administered and a sufficient amount of antibodies inhibited or decreased the endogenous PGCs in the recipient embryo. This is determined without sacrificing the embryos. Using Example 5 as an illustration, if there were none or fewer pigmented chicks produced then it is clear to one having skill in the art that there were fewer endogenous PGCs in the treated embryos.

Continuing, applicants submit there is no requirement that the determination of a decrease in PGC number itself be performed on every single treated embryo or that it be performed exclusively *in ovo*. Rather, and as set forth in the previous responses, the techniques disclosed for visualizing PGC numbers *in ovo* can be employed on a subset of treated animals, and the results of the tests performed on these avians can be extrapolated with a high degree of predictability to similar treated avians that are permitted to hatch. Here as well, the Patent Office fails to base its assertion of unpredictability on any reasonable scientific foundation, and thus this assertion does not support the instant rejection.

The Patent Office's maintained assertion that "[t]he ability to predict whether PGC numbers had decreased after immunizing an avian with an antigen was not described at the time of filing or in the specification; therefore, the ability to do so is 'unpredictable'" as set forth on page 8, lines 5-8, of the Official Action is believed to be

incorrect. Applicants direct the Patent Office's attention to Example 2 for evidence that the claimed treatments predictably reduce PGCs as set forth in the following sections from page 56:

> Immunizing females with individual peptides resulted in an approximately 35-55% reduction in endogenous PGC numbers, while immunization with two or more peptides simultaneously resulted in an approximately 55-70% reduction in endogenous PGCs.
>
> Statistical analysis. Treatment differences for the average number of PGCs/embryo were analyzed using the GLM procedure of the SAS System (SAS Institute Inc., Cary, North Carolina, United States of America). The model was PGC = treatment hen. Treatment differences were significant at $p < .0002$. (emphasis added)

Applicants respectfully submit that a demonstration of highly significant differences between treated and untreated avians ($p < 0.0002$ would be understood by one of ordinary skill in the art to be very highly significant) would show one of ordinary skill in the art that that treatment predictably reduces PGC numbers. Thus, contrary to the Patent Office's assertion, the instant specification does indeed inform one of ordinary skill in the art that "[t]he ability to predict whether PGC numbers had decreased after immunizing an avian with an antigen" was predictable.

The Patent Office's last contention regarding Assertion (B) is that "Applicants' arguments regarding using the methods to make chimeric chickens cannot be considered because such methods relate to a patentably distinct method, which applicants elected without traverse." (Official Action page 9, lines 11-13). Applicants respectfully submit that the Patent Office has presented no authority that supports the premise that not traversing a restriction is an admission/estoppel of any kind or that two restriction groups cannot share the same utility.

Additionally, applicants respectfully submit that after review of the instant specification, one of ordinary skill in the art would understand that a degree of germline chimerism (*i.e.*, the contribution of the donor PGCs to the recipient gonad) would be easily assayable by analyzing chimeric animals and/or by breeding the chimeras once they attain sexual maturity (as was demonstrated in Example 5). Applicants respectfully submit that standard molecular biology techniques can be employed for assaying

germline chimerism, and these assays can be performed on either interspecific chimeras or intraspecific chimeras.

To elaborate, routine techniques can be employed for isolating the terminal differentiated products of PGC differentiation (*i.e.*, the eggs and sperm of chimeric avians). With respect to both interspecific and intraspecific chimeras, routine genetic analysis can be employed to quantitate an extent of germline chimerism. Stated another way, easily assayable genetic differences exist between species and among different members of the same species, and these can be exploited to assay germline chimerism. The fact that these assays were not disclosed *per se* in the instant specification is irrelevant, since enablement analysis requires the Patent Office to consider what would have been within the routine ability of one of ordinary skill in the art (*see* M.P.E.P. § 2164.05(a), which states in part: "The specification need not disclose what is well-known to those skilled in the art and preferably omits that which is well-known to those skilled and already available to the public. *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987); and *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984)").

In view of the remarks above, and as demonstrated in Example 5 of the Specification, applicants respectfully submit that one of ordinary skill in the art would understand after review of the instant specification that standard breeding techniques could be employed to assay for germline chimerism. Applicants respectfully further submit that here, also, there is no requirement that the specification teach what is already known to, or would be understood by, one of ordinary skill in the art. The techniques that would be required for assaying germline chimerism by breeding chimeras are all routine in the field of animal husbandry, and since one of the consequences of reducing endogenous PGCs is that germline chimerism is enhanced (*see* the instant specification at page 1, line 31 to page 2, line 1), applicants respectfully submit that routine breeding experiments can be employed to confirm the effect of the immunizations if for some reason it were necessary.

The specification as filed indicates on page 1, line 31 to page 2, line 1, that chimerism can be increased by depleting endogenous PGCs. Routine comparisons can be employed to ensure that the treated embryos had reduced PGC numbers. The Patent Office has provided no reasonable scientific evidence to contradict the data explicitly set forth in the working examples of the instant specification that the methods of the pending claims successfully reduce PGC numbers and/or inhibit PGC development.

Therefore, for at least the reasons recited above, applicants respectfully submit that Assertion (B) fails to support the instant rejection.

And finally, in Assertion (C) the Patent Office contends that the specification does not enable using any antigen "associated with" PGCs as broadly claimed in claims 1 and 7. Applicants respectfully traverse.

Initially, without acquiescing to the contentions of the Patent Office and in an effort to advance prosecution, applicants respectfully submit that claims 1 and 7 have been amended to more clearly recite the claimed subject matter. As discussed with the claim amendments above, these claims have been amended to recite "antigen associated with primordial germ cells ~~development~~ development." Applicants respectfully submit that the amendments to claims 1 and 7 obviate this rejection.

Applicants note that Assertion (C) does not apply to claims 58-60 which are drawn to methods involving specific PGC antigens.

In addition, applicants submit that the specification as filed discloses a series of exemplary antigens associated with primordial germs cells, which include, but are not limited to SSAE-1, ovomucin-like protein (OLP), Steel Factor (c-kit ligand), germ cell-less, dead end, VASA (including, but not limited to the chicken VASA homolog, CVH), DAZL, nanos, stella, and fragilis polypeptides (*see* specification at page 11, line 27 to page 12, line 9). Given that the instant claims must be viewed from the perspective of one of ordinary skill in the art after review of the instant specification, applicants respectfully submit that one of ordinary skill in the art would also understand which antigens would represent appropriate antigens for use in the instantly claimed methods.

Therefore, even assuming *arguendo* that certain antigens might be undesirable for use in the instant methods, applicants respectfully submit that one of ordinary skill in

the art would understand which antigens would in fact be expected to be useful in the instant claims, the Patent Office has not presented a *prima facie* case of lack of enablement based on the fact that certain embodiments that fall within the scope of the claim might be inoperative. This is set forth in M.P.E.P. § 2164.08(b), which states in part:

> The presence of inoperative embodiments within the scope of a claim does not necessarily render a claim nonenabled. The standard is whether a skilled person could determine which embodiments that were conceived, but not yet made, would be inoperative or operative with expenditure of no more effort than is normally required in the art. *Atlas Powder Co. v. E.I. du Pont de Nemours & Co.*, 750 F.2d 1569, 1577, 224 USPQ 409, 414 (Fed. Cir. 1984)

Since applicants respectfully submit that with respect to antigens associated with PGC development, one of ordinary skill in the art "could determine which embodiments that were conceived, but not yet made, would be inoperative or operative with expenditure of no more effort than is normally required in the art", the Patent Office's assertion with respect to this point does not support the instant rejection.

Summarily, the Patent Office has employed an improper analysis in assessing the compliance of the instant claims with the enablement requirement of 35 U.S.C. § 112, first paragraph. None of the assertions presented in the Final Official Action establishes a *prima facie* case of non-enablement of claims 1, 7, or 58 and thus applicants respectfully request that the instant rejection be withdrawn at this time. Applicants further respectfully submit that claims 2-4, 8-10, and 59-60 all depend from one of claims 1, 7, or 58 and thus it is also believed that a *prima facie* case of non-enablement of these claims has not been presented.

Applicants submit that present claims 1, 7, and 58 are enabled under 35 U.S.C. 112, first paragraph. As a result, applicants respectfully request that the instant rejection of claims 1-4, 7-10, and 58-60 be withdrawn, and further that these claims be allowed at this time.

V. Response to the Indefiniteness Rejection

Claims 1-4, 7-10, and 58-60 have been rejected under 35 U.S.C. § 112, second paragraph, upon the contention that certain phrases appearing in the claims render the

claims indefinite. Particularly, the Patent Office has asserted that the phrases "sufficiently high concentration of antibodies that bind to the antigen expressed by an avian embryo within the egg to thereby decrease the PGC numbers [or development] in an avian embryo" in claims 1 and 7 is unclear. (Official Action, page 11, lines 4-7).

The Patent Office contends the phrase is indefinite because the specification allegedly does not teach how to determine whether PGC's decrease without sacrificing the avian and that applicants have not provided an assay for those of skill to determine when the amounts of antibodies were "sufficiently high" enough to decrease PGC numbers in an embryo that becomes a viable avian."

After careful consideration of the rejections and the Patent Office's bases therefor, applicants respectfully traverse the rejections and submit the following remarks.

The Patent Office contends that the specification does not teach how to determine whether PGC numbers decrease without sacrificing the avian, that the concentration of antibodies required to decrease the number or development of PGCs and maintain a viable embryo is not set forth in the specification or the art at the time of filing, and that the specification does not provide an assay for those of skill to determine when the amounts of antibodies were "sufficiently high" enough to decrease PGC numbers in an embryo that becomes a viable avian.

Applicants respectfully submit that these assertions are inaccurate and also do not support the instant rejection.

To elaborate, the Patent Office first contends that the specification does not teach how to determine whether PGC numbers decrease without sacrificing the avian. This assertion has been addressed in more detail hereinabove, and is believed to be inaccurate for at least the reasons stated in regard to Assertion (B) in Section IV above, which are incorporated here by reference. Further, applicants respectfully submit that whether or not the specification *per se* teaches how to do this, one of ordinary skill in the art would know several methods for accomplishing this goal upon a review of the instant specification. Therefore, one of ordinary skill in the art would easily be able to identify when a sufficiently high concentration of antibodies specific for the antigen to

decrease the PGC numbers or development in an avian embryo had occurred based on the guidance provided in the instant specification.

Next, the Patent Office asserts that the concentration of antibodies required to decrease the number or development of PGCs and maintain a viable embryo is not set forth in the specification or the art at the time of filing. This apparent requirement that a specific concentration be recited in the specification is believed to be clearly improper. Rather, applicants respectfully submit that all that is necessary is that one of ordinary skill in the art understand how to practice the methods of claims 1, 7, and 58 and understand when the methods of claims 1, 7, and 58 have been successfully executed. Given that all of the techniques required to assess the successful completion of the methods would be apparent to one of ordinary skill in the art based on the guidance provided in the instant specification, the instant assertion fails to support a rejection under 35 U.S.C. § 112, second paragraph.

And finally, the Patent Office asserts that the specification does not provide an assay for those of skill to determine when the amounts of antibodies were "sufficiently high" enough to decrease PGC numbers in an embryo that becomes a viable avian. Applicants respectfully submit that they have provided ample guidance in the instant specification as filed such that one of ordinary skill in the art would in fact have known how to assess PGC decreases in an avian that had hatched, (*e.g.* via breeding techniques) and thus for this additional reason, the instant assertion fails to support a rejection under 35 U.S.C. § 112, second paragraph.

Summarily, applicants respectfully submit that the phrase at issue is functional language that is perfectly acceptable under M.P.E.P. § 2173.01, which states in part:

> Applicant may use functional language, alternative expressions, negative limitations, or any style of expression or format of claim which makes clear the boundaries of the subject matter for which protection is sought. As noted by the court in *In re Swinehart*, 439 F.2d 210, 160 USPQ 226 (CCPA 1971), a claim may not be rejected solely because of the type of language used to define the subject matter for which patent protection is sought.

The Patent Office contends that the instant specification does not teach the means to assess the amount of antibodies without sacrificing the embryo. This

contention is refuted in the remarks above, particularly with respect to the teachings of Example 5 of the instant specification, which are incorporated here by reference.

Thus, the Patent Office has not presented a *prima facie* case of lack of compliance with 35 U.S.C. § 112, second paragraph, of claims 1, 7, and 58. Applicants further respectfully submit that claims 2-4, 8-10, and 59-60 all depend from one of claims 1, 7, or 58, and thus it is also believed that the instant rejection is inapplicable to these claims as well. As a result, applicants respectfully request that the instant rejection be withdrawn at this time.

As a result, applicants respectfully submit that claims 1, 7, and 58 fully comply with the requirements of 35 U.S.C. § 112, second paragraph, as reflected in M.P.E.P. § 2173.02 ("the examiner must consider the claim as a whole to determine whether the claim apprises one of ordinary skill in the art of its scope and, therefore, serves the notice function required by 35 U.S.C. 112, second paragraph, by providing clear warning to others as to what constitutes infringement of the patent"). Applicants further respectfully submit that claims 1-4, 7-10, and 58-60 are in condition for allowance, and respectfully solicit a Notice of Allowance to that effect.

VI. New Claims

New claims 69 -71 have been added. Support for the new claims can be found throughout the specification as filed, including particularly in the claims as originally filed (*see e.g.*, original claims 1). Additional support can be found in Example 1, particularly on page 52, lines 8-16, (sexually mature female birds were immunized with 50-200 µg of peptide antigen, including DAZL). As such, no new matter has been added by the inclusion of the new claims.

Applicants respectfully submit that new claims 69 -71 are believed to be in condition for allowance for at least the reasons set forth hereinabove with respect to the instantly pending claims.

As a result, applicants respectfully submit that claims 1-4, 7-10, 58-60, and 69-70 are in condition for allowance, and respectfully solicit a Notice of Allowance to that effect.

CONCLUSIONS

Should there be any minor issues outstanding in this matter, the Examiner is respectfully requested to telephone the undersigned attorney. Early passage of the subject application to issue is earnestly solicited.

DEPOSIT ACCOUNT

The Commissioner is hereby authorized to charge any fees associated with the filing of this correspondence to Deposit Account Number **50-0426**.

Respectfully submitted,
JENKINS, WILSON, TAYLOR & HUNT, P.A.

Date: 05/24/2010 By: _____

Arles A. Taylor, Jr.
Registration No. 39,395
Customer No. 25297
(919) 493-8000

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